Upregulation of Oct-4 isoforms in pulmonary artery smooth muscle cells from patients with pulmonary arterial hypertension.

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Public Summary:

Scientific Abstract:
Oct-4 is a transcription factor considered to be one of the defining pluripotency markers in embryonic stem cells. Its expression has also been demonstrated in adult stem cells, tumorigenic cells, and, most recently and controversially, in somatic cells. Oct-4 pseudogenes also contribute to carcinogenesis. Oct-4 may be involved in the excessive proliferation of pulmonary arterial smooth muscle cells (PASMC) in patients with idiopathic pulmonary arterial hypertension (IPAH), contributing to the pathogenesis of IPAH. In this study, we show that Oct-4 isoforms are upregulated in IPAH-PASMC. Human embryonic stem cells (H9 line) and human PASMC from normotensive subjects were used throughout the investigation as positive and negative controls. In addition to significant upregulation of Oct-4 in a population of IPAH-PASMC, HIF-2alpha, a hypoxia-inducible transcription factor that has been shown to bind to the Oct-4 promoter and induces its expression and transcriptional activity, was also increased. Interestingly, a substantial upregulation of Oct-4 isoforms and HIF-2alpha was also observed in normal PASMC exposed to chronic hypoxia. In conclusion, the data suggest that both Oct-4 isoforms are upregulated and potentially have a significant role in the development of vascular abnormalities associated with the pathogenesis of IPAH and in pulmonary hypertension triggered by chronic hypoxia.